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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/944,432	08/30/2001	Kevin P. Baker	P2548P1C5	2341

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EXAMINER
KAUFMAN, CLAIRE M

ART UNIT	PAPER NUMBER
1646	9

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/944,432	BAKER ET AL.	
	Examiner	Art Unit	
	Claire M. Kaufman	1646	

-- The MAILING DATE of this communication appears on the cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/39/01 and 9/5/02* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Trademarks

The use of the trademark "American Type Cell Culture" has been noted in this application on page 147. It should be capitalized wherever it appears and be accompanied by the generic terminology or include a proper trademark symbol: AMERICAN TYPE CELL CULTURE or American Type Cell Culture™.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22, 27 and dependent claims 23-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22 and 27 are indefinite because claim 22 recites "binds" and claim 26 recites "specifically binds". Absent a definition of "specific binding" it is not clear what the difference between the two claims is and what each claim is meant to encompass, given that antibody binding is determined by the variable regions structure and is a "specific" event.

Claim Rejections - 35 USC §§ 101/112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

> pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-27 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are drawn to an antibody that binds a polypeptide of SEQ ID NO:32. While the encoding nucleic acid which has the sequence of SEQ ID NO:31 has utility as a diagnostic marker for colon tumor (see Table 13, p. 129), the encoded polypeptide and binding antibody have no such utility since there is no reason to suspect that there is alteration of polypeptide sequence or amount in colon tumor *versus* normal tissue. If the antigen does not have utility, the antibody that binds that antigen likewise does not have utility. Even if the DNA has utility as a colon tumor marker, the encoded protein does not have utility because it is not known what the protein does or if the level of PRO327 protein in colon tumors corresponds to nucleic acid transcript level, *i.e.*, if an increased gene amplification in colon tumors corresponds to an increased amount of expressed protein. It does not necessary follow that an increase in gene copy number results in increased gene expression and increased protein expression, such that the polypeptide would be useful diagnostically or as a target for cancer drug development. For example, Pennica et al. (1998, PNAS USA 95, p.14722, second paragraph) teach that:

> An analysis of WISP-1 gene amplification and expression in human coon tumors showed a correlation between DNA amplification and overexpression, whereas overexpression of WISP-3 RNA was seen in the absence of DNA amplification. In contrast, WISP-2 DNA was amplified in colon tumors, but its mRNA expression was significantly reduced in the majority of tumors compared with expression in normal colonic mucosa from the same patient.

Additionally, Hayes et al. (Electrophoresis 19 :1862-1871, 1998) studied 80 proteins relatively homogenous in half-life and expression level, and found no strong correlation between protein and transcript levels; for some genes, equivalent mRNA levels translated into protein abundances which varied by more than 50-fold. It was concluded that the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript (p. 1863, second paragraph, and Figure 1). Therefore, because it cannot be concluded that the PRO327 is associated with formation or growth of colon tumor or is useful itself as a diagnostic marker for colon cancer, the encoded protein does not have utility. Significant further research would be required to find out

what the protein does and if and how it is linked to lung and/or colon cancer. Therefore, the same or more further research would be required to use the binding antibody.

The specification states (p. 101, lines 9-11) that "PRO327 possess significant homology to the human prolactin receptor protein, thereby indicating that PRO3217 may be a novel prolactin receptor protein." (See also, p. 4, lines 16-17.) Expression of PRO327 nucleic acid in mouse and human fetus was found in lung (paragraph bridging pages 145-146), leading to the speculated function of "Probable role in bronchial development." It does not appear to have any significant expression in adult tissues (p. 142, Table 24, and p. 146, lines 1-9). The cDNA was originally obtained by using PCR primers based on ESTs structurally related to human prolactin receptor (Example 8 beginning on page 100). Neither the showings of the specification nor the art support assignment of PRO327 to the prolactin receptor family. According to Applicants BLAST results, #5 (A10-A12) shows 99% identity with a described "Human U4 haematopoetin receptor" related encoding nucleic acid. PRO327 (SEQ ID NO:32) shows only 14.5% identity to a known prolactin receptor (Figure1, Hu et al., J. Biol. Chem., 276(44):41086-94, 2001, see "SEQUENCE COMPARISION HU" attached). An interleukin-6 receptor (IL-6R) shows 14.1% identity with PRO327 (Figure 2B, Hibi et al., Cell 63:1149-1157, 1990, see "SEQUENCE COMPARISION HIBI" attached), which is virtually the same identity shared with the prolactin receptor. Further, it shows 100% identity with prior art "Cytokine-Like Factor-1 (Figure 1A, Elson et al., J. Immunol. 161:1371-9, 1998, see "SEQUENCE COMPARISION ELSON" attached). EMBL entry AAD54385 shows a protein 99.8% identical to PRO327 and labeled as "Class I cytokine receptor" (see "SEQUENCE COMPARISION EMBL" attached). As can be seen from the variety of proteins sharing structural identity with PRO327, one skilled in the art could not assign PRO327 to the prolactin receptor or other defined family that would allow the skilled artisan to know how to specifically and substantially use it. For these reasons, there is no substantial and specific utility for the antibody that binds the protein PRO327.

Claims 22-34 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Because it would require significant further experimentation to be able to use the claimed antibody because no definite function has been determined for the PRO327 protein which it binds and there is no definite function supported by the prior art. No function can be reasonably assigned based on SEQ ID NO:32 homology to another protein(s). Even though the PRO327 nucleic acid can be used as a diagnostic for colon tumor, the encoded polypeptide and antibody cannot be used diagnostically since there is no known or reasonably expected alteration of polypeptide sequence or amount in colon tumor.

35 U.S.C. §§ 102/103

The following rejections under 35 U.S.C. §§ 102 and 103 are made under the assumption that the effective filing date for the instantly claimed invention is 08/30/2001, which is the actual filing date of the instant application. Applicant is advised that the instant application can only receive benefit under 35 U.S.C. §120 from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, with respect to the new claimed invention. Because the instant application does *not* meet the requirements of 35 U.S.C. § 112, first paragraph, for the reasons given above and it is a continuing application of Serial Number 09/866,028, the prior application also does not meet those requirements and, therefore, is unavailable under 35 U.S.C. § 120.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 22, 26 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Elson et al. (J. Immunol. 161:1371-1379, 1998).

Elson et al. teach Cytokine-Like Factor-1 (CLF-1) which has a sequence identical to SEQ ID NO:32 of the instant application (see "SEQUENCE COMPARISION ELSON" attached). Also taught are monoclonal antibodies that specifically bind CLF-1 (p. 1373, col. 1, third-sixth

paragraphs). Also taught are the antibodies labeled with horseradish peroxidase (p. 1373, col. 1, "Detection of hCLF-1 by Western blot analysis").

Note the specification does not have a limiting definition of "labeled" antibody (claim 26). The specification describes examples of labeling, including indirect labeling (p. 89, lines 8-20).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elson et al. as applied to claims 22, 26 and 27 above, and further in view of Godowski et al. (US Patent 6,030,831).

Elson et al. is relied upon for the teachings set forth above. Elson et al. do not teach a humanized antibody or an antibody fragment. Antibodies were used for protein detection (Figure 6). Elson et al. also suggesting determining if a ligand binds the hCLF-1 (sentence bridging pages 1377-1378). Beginning 5 lines from end of page 1373 through the first sentence of page 1375, it was concluded, "This suggests that the cloned human and mouse cDNAs encode soluble proteins." Elson et al. does not teach antibody fragments, humanized antibodies or directly labeled antibodies.

Godowski et al. teach general methods of producing and using antibodies including monoclonals, fragments (col. 13, line 47-60), labeled (col. 16, lines 38-48) and humanized

antibodies (col. 14, lines 7-33, and col.17, line 17-col. 18, line 6) to secreted proteins (related to TIE ligands). Godowski et al. teach (col. 16, lines 55-59) such antibodies "...may be employed for any know assay method, such as competitive binding assays, direct and indirect sandwich assays, and immunoprecipitation assays." The assays are also described (col. 16, line 55-col. 17, line 17).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the antibodies of Elson et al. such as labeled or humanized antibodies or antibody fragments because Godowski et al. teach a variety of antibody types directed to a soluble protein, as is hCLF-1 of Elson, and useful methods of making and using them. One would have been motivated to make such antibodies to use in protein localization, for example, or to identify a binding partner or ligand of the protein.

Conclusion

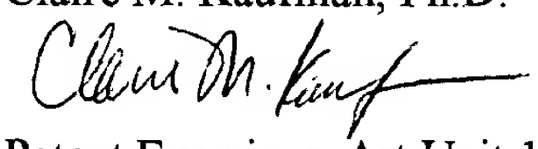
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791. Dr. Kaufman can generally be reached Monday through Thursday from 8:30AM to 12:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (703) 308-6564.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.



Patent Examiner, Art Unit 1646

May 15, 2003